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Original Research Article

A study of thyroid profile in chronic liver disease patients attending a tertiary care center in Kumaon region of Uttarakhand

Vivekanand Satyawali[1]*, Seema Gupta[2], Yogesh Kumar[3], Devansh Satyawali[4]

[1]*Dept. of Medicine, Government Medical College, Haldwani, Uttarakhand, India*
[2]*Dept. of Biochemistry, Government Medical College, Haldwani, Uttarakhand, India*
[3]*Dept. of Medicine, Government Medical College, Haldwani, Uttarakhand, India*
[4]*Vardhman Mahavir Medical College, Delhi, India*

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ABSTRACT

Introduction: The liver is crucial for the metabolism of thyroid hormone and production of thyroxine-binding globulin production (TBG). Liver dysfunction can result from changes in thyroid function, and distinct liver conditions can have different impacts on the metabolism of thyroid hormones
Objectives: This study tries to find out the relationship between thyroid function and liver disease.
Materials and Methods: The cross-sectional, institution-based observational study from January 2020 to September 2021. The study population included patients with chronic liver disease who visited the OPD or were admitted to the medical wards of Dr. Susheela Tiwari memorial hospital, a tertiary care hospital of Kumaon region of Uttarakhand. The study proforma included the demographic data, history, clinical examination and details of investigations. Tests performed included Complete Hemogram, Liver function tests, Serum creatinine, Blood urea, Serum electrolytes, Abdominal ultrasound, Prothrombin time, INR and thyroid function tests.
Results: Mean serum T3 and T4 level didn't follow any uniform trend with the severity of disease, however mean TSH increased with the increase in the severity of the disease. Although this was not found to be statistically significant.
Conclusion: The thyroid dysfunction holds an important place in the spectrum of Chronic liver disease. Progressive worsening of liver function increases likely hood of abnormal underlying thyroid dysfunction and therefore, patients need to be evaluated for thyroid dysfunction periodically.

1. Introduction

Liver is a vital organ in human body. The formation of transport proteins and the hormonal metabolism are the main functions of the liver. The prevalence of liver disease is already very high both globally and in India and it is expected to rise much further in the future.[1] Liver diseases can have various associated endocrine disturbances.

The liver plays crucial role in thyroid hormones metabolism through conjugation, excretion, peripheral deiodination, and production of thyroxine-binding globulin (TBG). Liver dysfunction can result from changes in thyroid function, and distinct liver conditions can have different impacts on the metabolism of thyroid hormones.[2,3] Because of the toxic consequences and indirectly because of the altered production of carrier proteins, liver failure results in a secondary dysfunction of the endocrine glands. In light of this, symptoms of an apparent hormonal imbalance may also accompany chronic liver disease.

Tri-iodothyronine and thyroxine are necessary for healthy growth, development, and operation of various organs of human body and these control the basal metabolic

* *Corresponding author*.
E-mail address: vivek_satyawali@yahoo.co.in (V. Satyawali).

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rate of all cells, including hepatocytes thereby impacting liver function. The liver is crucial for the conjugation, peripheral deiodination, and production of thyroid binding globulin that occur during the metabolism of thyroid hormones.[4–6] Hence, it is common to encounter thyroid dysfunction in various spectra of liver disease and has relation with the severity of liver disease.[7,8]

Numerous investigations examining thyroid status in individuals with liver disease have been conducted, primarily in Japan and Europe. The number of patients in which these investigations have been undertaken limits the majority of them. In the context of a tertiary care hospital in northern India, the goal of this study is to determine the relationship between thyroid function and liver disease.

2. Materials and Methods

The study was conducted in Department of Medicine of Dr. Sushila Tiwari memorial Hospital, Government Medical College's in Haldwani (Uttarakhand). The study design was cross-sectional institution-based observational study performed between January 2020 to September 2021. The study population included patients with chronic liver disease (CLD) who visited the OPD and were admitted to the hospital's medical wards. Patients aged more than 16 years, patients attending our institution with known cases of CLD, and newly diagnosed CLD patients attending our hospital as OPD/IPD, patients willing to participate in the study were included in the study. Patients having known thyroid disease and patients unwilling to participate were excluded. The study proforma included the demographic data, history, clinical examination and details of investigations. Tests performed were Complete Hemogram, Liver function tests, Serum creatinine, Blood urea, Serum electrolytes, Abdominal ultrasound, Thyroid function tests Prothrombin time, and INR,. Patients were labeled as CLD if they have positive history of significant alcohol drinking, or risk factors of CLD, with clinical examination suggestive of CLD, like splenomegaly, ascites, hepatomegaly, varices, spider angioma palmer erythema, and symptoms of hepatic encephalopathy. These patients were further subjected to biochemical and radiological test to confirm CLD. Hepatomegaly, blunted liver margins, an uneven liver surface, and a coarse liver texture were among the radiological findings.

3. Results

Table 1 a total 100 patient were included in study; males were in more in number 71(71.0%) among the study participant as compared to females 29 (29.0%) and majority of the study subjects (73.0%) were in the age group 41 – 60yrs followed by 18 – 40yrs (19.0%) and >60yrs (8.0%).

Table 2 shows mean of different blood parameter in the study subjects. Mean Hb was 10.04±3.29mg/dl, mean TLC was 9524.42±5012.82, mean Platelet was 1.18±0.54, mean PT was 18.41±4.46, mean INR was 1.42±0.36, mean Total serum bilirubin was 2.89±3.07, mean Direct serum bilirubin was 1.93±2.35, mean ALP was 236.59±190.07, mean SGOT was 222.80±409.76, mean SGPT was 167.53±194.97, meanS.Creatinine was 1.31±0.84, mean B. Urea was 44.84±30.31 and mean S. Albumin was 2.99±0.57.

Table 3 shows that mean T3 was 1.31±0.75, mean T4 was 6.53±2.58 and mean TSH was 5.06±2.59 for the study subjects.

Table 4 shows that among the different risk factors of CLD, alcohol intake was present in maximum numbers of study participants(63%), followed by HCV infection(30%), HbsAG positivity (16%), H/O blood transfusion(25%), multiple sexual partners(8%), needle stick injury(5%) and intake of herbal preparations (5%)

Study subjects were also categorized according to child pugh severity grade of disease, out of total 100 subjects, 49(49%) subjects were in class B, 45 (45%) subjects in class C, and 6(6%) patient in class A child pugh severity grade. Table 5 shows that mean serum T3 and T4 level didn't followed any uniform trend with the severity of disease, however mean TSH increased with the increase in the severity of the disease. Although this was not found to have statistical significance.Table 5

4. Discussion

In the present study, 100 patients with chronic liver disease participated. A thorough history and medical examination, hematological and biochemical tests, ultrasound and thyroid profile done in all cases. The relationship between thyroid hormones (TSH, T3, and T4) and Child Pugh score was assessed.

This study enrolled 100 patients with chronic liver disease with a mean age of 49±9.1 years (range 30-75 years). The mean age of patients in studies by Punekar P et al[9] was 43±14 years, and Kumar KH et al[10] was 55.4±11.9 years. It was observed that most of the patients were in the age group of 41 to 60 years. In our study, male (71%) cases were more compared to female (29%), this difference in gender distribution may be attributed to increased prevalence of alcoholism among males in this geographic area leading to more prevalence of chronic liver disease. Similar differences in gender distribution were found in various other studies.

Alcohol intake was present in maximum number of study subjects (63.0%), %), followed by HCV infection (30%), HbsAG positivity (16%), H/O blood transfusion(25%), multiple sexual partners (8%), needle stick injury (5%) and intake of herbal preparations (5%). Harish A Rao[11] also observed significant alcohol intake history in cases as compared to the control (p=0.007). The mean years of consumption alcohol was also significantly high in the cases

Table 1: Distribution of study participant by gender and age group

Gender	Number	%
Male	71	71.0
Female	29	29.0
Age Group		
18 – 40yrs	19	19.0
41 – 60yrs	73	73.0
>60yrs	8	8.0

Table 2: Mean Blood parameters of the study subjects

Blood parameter	Mean	SD	Minimum	Maximum
Hb (gm/dl)	10.04	3.29	2.4	15.6
TLC(x1000/ul)	9524.42	5012.82	1400	28000
Platelet(x1000/ul)	1.18	0.54	0.30	3.20
PT	18.41	4.46	13.0	40.0
INR	1.42	0.36	1.00	3.30
Total Serum Bilirubin (mg/dl)	2.89	3.07	0.4	18.7
Direct Serum Bilirubin (mg/dl)	1.93	2.35	0.10	14.00
ALP (u/l)	236.59	190.07	19.0	1141.0
SGOT(u/l)	222.80	409.76	16.0	3449.0
SGPT(u/l)	167.53	194.97	11.0	1389.0
S. Creatinine (mg/dl)	1.31	0.84	0.5	6.4
B. Urea(mg/dl)	44.84	30.31	16.0	189.0
S. Albumin(mg/dl)	2.99	0.57	1.00	4.00

Table 3: Mean Thyroid profile parameters of the study subjects

Parameter	Mean	SD	Minimum	Maximum
T3	1.31	0.75	0.11	4.30
T4	6.53	2.58	0.58	14.20
TSH	5.06	2.59	0.45	14.98

Table 4: -Distribution of study subjects according to risk factors

Risk factors		Numbers (n)	Percent %
Alcohol	Present	63	63
	Absent	37	37
HCV	Present	30	30
	Absent	70	70
HbsAg	Present	16	16
	Absent	84	84
H/O blood transfusion	Present	25	25
	Absent	75	75
Multiple sexual partner	Present	8	8
	Absent	92	92
Needle stick injury	Present	5	5
	Absent	95	95
Herbal preparations	Present	5	5
	Absent	95	95

Table 5: Comparison of Thyroid profile parameter with severity of disease

Thyroid profile parameter	Severity of disease	Mean	SD	P value*
T3 (Normal refence range 0.85-2.02 ng/ml)	Class A	1.37	0.61	
	Class B	1.28	0.73	0.90
	Class C	1.34	0.81	
T3 (Normal refence range 5.13-14.06 microgram/dl)	Class A	7.29	0.98	
	Class B	6.37	2.59	0.71
	Class C	6.58	2.73	
T3 (Normal refence range 0.27-4.20 micro IU/ml)	Class A	4.28	1.52	
	Class B	4.77	1.93	0.33
	Class C	5.47	3.23	

(p=0.033). Study by Chaudhary S et al[12] suggested that common cause of cirrhosis was ethanol ingestion which was found in 97 (88.18%) patients and chronic hepatitis B infection was the second most common cause.

In our study mean ALP was 236.59±190.07, mean SGOT was 222.80±409.76, mean SGPT was 167.53±194.97, which were higher than the normal range and mean S. Albumin was 2.99±0.57 which was on lower side. Similar to our study Deepika G[13] also observed raised serum ALT (mean range is 109±103) raised AST (mean range 84.9± 86.4) and raised serum ALP (mean is 159±139) in study population. While contrary to our study there was no significant difference in the mean range levels of total protein 7.57±5.58, and albumin 4.12±2.53. In contrast to our study, study by Kumar M[14] on CLD by chronic hepatitis B infection showed normal ALT, defined as less than 40 U/L, and found histological disease activity in 14% to 40%, depending on e antigen status. Despite the liver's tremendous capacity for regeneration, chronic liver injury can result in fibrosis and eventually end-stage liver disease. Classically, aminotransferase elevation is interpreted as a marker of hepatocellular damage.[15] This was also detected in the study by Bebars GM et al[16] where all the three groups with liver disease showed a significant elevation in liver enzymes levels (ALT & AST). Wang L et al[17] similarly observed that patients with type A HE showed higher levels of aspartate aminotransferase (AST) and bilirubin.

Kharb S et al[18] studied thyroid function in over 75 patients with acute hepatitis, chronic liver disease and liver transplant group and concluded that patients with liver transplant, chronic liver disease and acute hepatitis groups, had significantly lower total T3 compared with healthy controls. Study by Oren R et al[19] showed that hypothyroidism was also associated with lesser degrees of decompensation in cirrhosis. Therefore, controlled induction of hypothyroidism might prove beneficial in cirrhotic patients, but more robust data and studies are required to establish this hypothesis. Also, a state of hypothyroidism has been seen in stable cirrhosis patients that correlates with slow progression of stage of cirrhosis.[17]

In our study there was inverse correlation between T3and T4 levels and Child Pugh score. i.e. low T3 and T4 levels were associated with high Child Pugh score and vice versa. However, this correlation was not found to be significant. There was non-significant positive correlation between TSH and Child Pugh score (p value of 0.33). i.e., high TSH was associated with high Child Pugh score and vice versa.

Mansour-Ghanaei F et al[20] reported a negative correlation between Child Pugh scores and total serum T3 level ($r = -0.453$, $P < 0.001$). The study also observed a reverse correlation between MELD score and T3 levels ($r = -0.305$, $P = 0.14$) and concluded that serum T3 levels are good index of hepatic function, which decrease with the severity of liver damage.

Mousa et al[21] reported that there was a significant decrease level of T3 (p value <0.05) in cirrhotic patients compared to controls as was seen with Borzio M et al[8] who on evaluating thyroid function in 33 patients with liver disease observed that levels of T3, FT3 and T3/thyroxine binding globulin and thyrotropin after thyrotropin releasing hormone administration were significantly reduced.

5. Conclusion

Firstly in chronic liver disease patients there is a significant occurrence of hypothyroidism. Secondly, there exists a negative correlation between tri-iodothyronine and Child-pugh score. The present study revealed that thyroid dysfunction is more prevalent in cirrhotic patients specially hypothyroidism and there are several reasons of it. The liver plays an important role in metabolism of thyroid hormone because thyroid-binding globulin (TBG), prealbumin and albumin being binder of thyroid hormones are synthesized in liver. It is also responsible for thyroid hormone peripheral metabolism. Liver is involved in the conjugation, biliary excretion, oxidative deamination and the extra thyroidal deiodination of thyroxine (T4) to triiothyronine (T3) and to reverse T3. Also, the level of thyroid hormone is important for normal hepatic function and bilirubin metabolism. In conclusion, thyroid dysfunction has an important place in the spectrum of Chronic liver disease. Thyroid dysfunction is a frequent occurrence in a patient with deteriorating liver function and these patients should be evaluated for thyroid dysfunction periodically.

6. Source of Funding

None.

7. Conflict of Interest

None.

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Author biography

Vivekanand Satyawali, Associate Professor https://orcid.org/0000-0001-9946-8460

Seema Gupta, Assistant Professor https://orcid.org/0000-0001-8208-3564

Yogesh Kumar, Post Graduate

Devansh Satyawali, Final Year Student https://orcid.org/0000-0001-6182-0502

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